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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/604,400	07/17/2003	Eric T. KOOL	12665.0024.NPUS01	1399

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EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	**PAPER NUMBER**
1637	

MAIL DATE	DELIVERY MODE
12/19/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/604,400	KOOL, ERIC T.	
	Examiner	Art Unit	
	TERESA E. STRZELECKA	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2008 and 06 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,16-27 and 29-50* is/are pending in the application.

4a) Of the above claim(s) *16-27 and 29-39* is/are withdrawn from consideration.

5)☒ Claim(s) *40-49* is/are allowed.

6)☒ Claim(s) *1-14 and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after a decision by the Board of Patent Appeals and Interferences, but before the filing of a Notice of Appeal to the Court of Appeals for the Federal Circuit or the commencement of a civil action. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on August 11, 2008 has been entered.

2. All of the previously presented rejections are withdrawn in view of Applicant's amendments and the decision rendered by the Board of Appeals.

3. Claims 1-49 were previously pending, with claims 16-39 withdrawn from consideration. Applicants amended claims 1, 16, 21, 23, 25, cancelled claims 15 and 28 and added claim 50. Claims 1-14, 16-27 and 29-50 are pending, with claims 16-27 and 29-39 withdrawn from consideration. Claims 1-14 and 40-50 will be examined.

4. Applicant's arguments are moot in view of new grounds of rejection.

Claim Interpretation

5. Applicant did not define the term "fluorescence quenching leaving group", therefore it is interpreted as any fluorescence quenching group.

6. Applicant did not define what it means for the fluorescence to be quenched. For example, in the case of a fluorescence donor-acceptor pair, the fluorescence intensity of the donor usually decreases in the presence of the fluorescence acceptor, therefore in this case the acceptor is considered as a fluorescence quencher.

7. Applicant did not define the terms “about 2 fold”, “about 100 fold” and “about 1000 fold”, therefore any value of the quenching is considered as anticipating these terms, since the degree of quenching depends on the proximity of the two dye molecules, solution conditions and the spectral overlap of the emission and absorption spectra of the two dyes.

8. The term "leaving group" has not been defined. Further, this is a functional, not a structural limitation, since for every chemical bond there is a nucleophile and a set of conditions under which the bond can be broken. Finally, "leaving" simply means getting separated from the probe, which can be achieved by enzymatic cleavage, for example.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 2-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms: "efficiency of quenching of at least 2 fold" in claim 2, "efficiency of quenching of at least 100 fold" in claim 3 and "efficiency of quenching of at least 1000 fold" in claim 4 are relative term which render the claims indefinite. The term "at least x fold" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Since the term "efficiency of quenching of at least 2 fold" (or 100 fold or 1000 fold) refer to a particular set of conditions and fluorophore-quencher combination, and there is no reference to a state relative to which the efficiency of quenching is determined, these terms are indefinite.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-7, 9-12, 14 and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Aoyagi et al. (U.S. Patent No. 5,952,202 A).

Regarding claims 1 and 50, Aoyagi et al. teach a nucleic acid probe comprising a fluorophore and a quencher (Fig. 1; col. 4, lines 38-67; col. 5, lines 1-15; col. 8, lines 10-31). Aoyagi et al. teach dabsyl as a quencher (col. 9, lines 33-38; Fig. 3).

Regarding claims 2-4, Aoyagi et al. teach dabsyl as a quencher (col. 9, lines 33-38; Fig. 3). Therefore, since the limitations of the efficiency of quenching are not structural limitations, they are anticipated by the structure claimed.

Regarding claims 5-7, Aoyagi et al. teach single-stranded nucleic acids (col. 15, lines 14-27; Fig. 1, 4).

Regarding claim 9, Aoyagi et al. teach attaching the quencher to the 5' end of the probe (col. 8, lines 57-62; col. 16, lines 37-46).

Regarding claim 10, Aoyagi et al. teach attaching the quencher to the 3' end of the probe, i.e. at a site different from the 5' hydroxyl (col. 8, lines 57-62).

Regarding claim 11, Aoyagi et al. teach separation of the fluorophore and quencher by about 10-100 angstroms (col. 15, lines 50-52). Since the distance between two base pairs is 3.4 angstroms, Aoyagi et al. inherently teach separation of the fluorophore from the quencher by 3 or more nucleotides.

Regarding claim 12, Aoyagi et al. teach DNA or RNA probes (col. 16, line 20). Therefore, since nucleic acid bases contain NH groups, Aoyagi et al. inherently teach nucleophilic groups. Further, RNA possesses 2' hydroxyls, again, nucleophilic groups. Finally, in case where the 3' terminal hydroxyl of the probe is not attached to either the fluorophore or the quencher (col. 15, lines 60-65), the hydroxyl is free and is a nucleophile.

Regarding claim 14, Aoyagi et al. teach fluorescein, JOE, TAMRA, ROX (col. 9, lines 25-36).

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Aoyagi et al. (U.S. Patent No. 5,952,202 A) and Lee et al. (U.S. Patent No. 6,348,596 B1).

A) Aoyagi et al. teach single-stranded TaqMan probes, but do not teach double-stranded probes.

B) Lee et al. teach fluorescently-labeled energy-transfer probes which can be either single-stranded or double-stranded (Fig. 5B-5E; col. 59, lines 19-67; col. 60; col. 61, lines 1-36).

Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used alternative label configurations suggested by Lee et al. in the fluorophore-quencher detection system of Aoyagi et al. As stated by MPEP 2144.06:

2144.06 Art Recognized Equivalence for the Same Purpose [R-6] - 2100 Patentability

>II. < SUBSTITUTING EQUIVALENTS KNOWN FOR THE SAME PURPOSE

In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. *In re Ruff*, 256 F.2d 590, 118 USPQ 340 (CCPA 1958) (The mere fact that components are claimed as members of a Markush group cannot be relied upon to establish the equivalency of these components. However, an applicant's expressed recognition of an art-recognized or obvious equivalent may be used to refute an argument that such equivalency does not exist.); ** *Smith v. Hayashi*, 209 USPQ 754 (Bd. of Pat. Inter. 1980) (The mere fact that phthalocyanine and selenium function as equivalent photoconductors in the claimed environment was not sufficient to establish that one would have been obvious over the other. However, there was evidence that both phthalocyanine and selenium were known photoconductors in the art of electrophotography. "This, in our view, presents strong evidence of obviousness in substituting one for the other in an electrophotographic environment as a photoconductor." 209 USPQ at 759.).

An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982).

15. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Aoyagi et al. (U.S. Patent No. 5,952,202 A) and Mayrand (U.S. Patent No. 5,691,146 A).

A) Regarding claim 13, Aoyagi et al. teach blocking the 3' end of the probe with phosphate group or a fluorophore to prevent the probe being extended during the reaction (col. 16, lines 46-55), but do not teach phosphorothioate group.

B) Mayrand teaches self-quenching probes used in real-time PCR assays (Abstract; Fig. 1). Mayrand discloses that it is preferable to block the 3' end of the probe so that it is not extended during the amplification reaction, and teach using phosphorothioate groups to achieve this result (col. 6, lines 18-41).

Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the alternative means for blocking the 3' terminus of the probe suggested by Maynard in the method of Aoyagi et al. As stated by MPEP 2144.06:

2144.06 Art Recognized Equivalence for the Same Purpose [R-6] - 2100 Patentability

>II. < SUBSTITUTING EQUIVALENTS KNOWN FOR THE SAME PURPOSE

In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. *In re Ruff*, 256 F.2d 590, 118 USPQ 340 (CCPA 1958) (The mere fact that components are claimed as members of a Markush group cannot be relied upon to establish the equivalency of these components. However, an applicant's expressed recognition of an art-recognized or obvious equivalent may be used to refute an argument that such equivalency does not exist.); ** *Smith v. Hayashi*, 209 USPQ 754 (Bd. of Pat. Inter. 1980) (The mere fact that phthalocyanine and selenium function as equivalent photoconductors in the claimed environment was not sufficient to establish that one would have been obvious over the other. However, there was evidence that both phthalocyanine and selenium were known photoconductors in the art of electrophotography. "This, in our view, presents strong evidence of obviousness in substituting one for the other in an electrophotographic environment as a photoconductor." 209 USPQ at 759.).

An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982).

16. No references were found teaching or suggesting claims 40-49, therefore these claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA E. STRZELECKA whose telephone number is (571)272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Primary Examiner
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December 16, 2008